DR. TIMOTHY J. YEATMAN

Dr. Timothy J. Yeatman, F.A.C.S, is the Associate Center Director for Translational Research and Director of Total Cancer Care at H. Lee Moffit Cancer Center and Research Institute. In this role, he has responsibility for developing translational research at Moffitt by leading the infrastructure development and implementation of Total Cancer Care (TCC). The successful implementation of TCC involves collaborations with many areas of the Cancer Center such as information technology, health outcomes and behavior, and the expansion of tumor banking, tissue microarray, and gene expression profiling capabilities. In addition, Dr. Yeatman, working with Adil Daud, M.D., oversees the Affiliate Research Program and continued expansion of translational research trials at Moffitt affiliate sites throughout the state. He joined the Moffitt Cancer Center in 1992.

Dr. Yeatman has focused his research on the management of gastrointestinal malignancies with a special research emphasis on using genome scale microarrays to identify the molecular signatures of cancer that provide diagnosis, prognosis and response to therapy. He recently compared microarray data of 540 human tumors of 21 different tumor types with the diagnoses obtained from tumor biopsies. He found that microarray was 88 percent accurate in predicting all tumor types. The results of his investigation, the first such work to be reported in this depth, appeared in the January 2004 issue of the American Journal of Pathology. In addition, he and his colleagues have detected 340 new tumor markers and more than 100 tumor progression markers whose expression correlated with progressing tumor stage. Some of these markers may be useful in the clinical management of colon cancer patients because of their capacity to detect and predict the stage of cancer.

He has published more than 115 articles in the top peer-reviewed journals in his field including the prestigious *Nature Genetics*, *Nature Reviews Cancer,* as well as the *Journal of the National Cancer Institute*, and *Cancer Research.* He has received numerous honors and awards including the James IV Association of Surgeons Traveling Fellowship, Europe 2001; the Center Director's Award for Outstanding Research at Moffitt Cancer Center (1998, 1997, 1995); and the James Ewing Foundation Trainee Award, Society of Surgical Oncology, 1997.

TOTAL CANCER CARE CONSORTIUM

"Discover, Translate, Deliver Personalized Cancer Care"

Timothy J. Yeatman, M.D., FACS
Professor of Surgery & Interdisciplinary Oncology
Associate Center Director for Translational Research
Director, TCC
H. LEE MOFFITT CANCER CENTER

The Problem with Contemporary Cancer Care

- Many patients are treated to help an unknown few—one size fits all
- Drug therapy is generally not tailored to the patient
- Response rates low, toxicity high
- Patients do not want to leave home for treatment

The Solution:

Total Cancer Care Consortium: a Statewide Enterprise Effort

(Academic + Community)

A research project that will lead to *personalized* cancer care by 2010

Research → Practice

Total Cancer Care | Personalized Cancer Care | 2010

Study large populations…

Develop therapies for Subpopulations of individuals…

What is TCC?

- Perhaps the worlds largest translational research project
- A means to collect, relate, and interpret clinical data and molecular data from thousands of patients across Florida
  - Tumor and blood samples
  - Clinical data (risk factors, therapies, responses, survival)
- A mechanism to identify molecular signatures for diagnosis, prognosis, and prediction of response to therapy
- A means to personalize cancer therapy by matching "pipeline" drugs to patients harboring molecular targets
- A means to improve the quality of medicine

Hypothesis/Plan

- Identify drug-specific molecular targets (or surrogate for it)
- Determine prevalence of targets in large Florida database
- Enrich pipeline drug trials with Florida patients harboring the target
- Engage and invest in community and academic partners to achieve necessary accrual
- Decrease time to drug registration

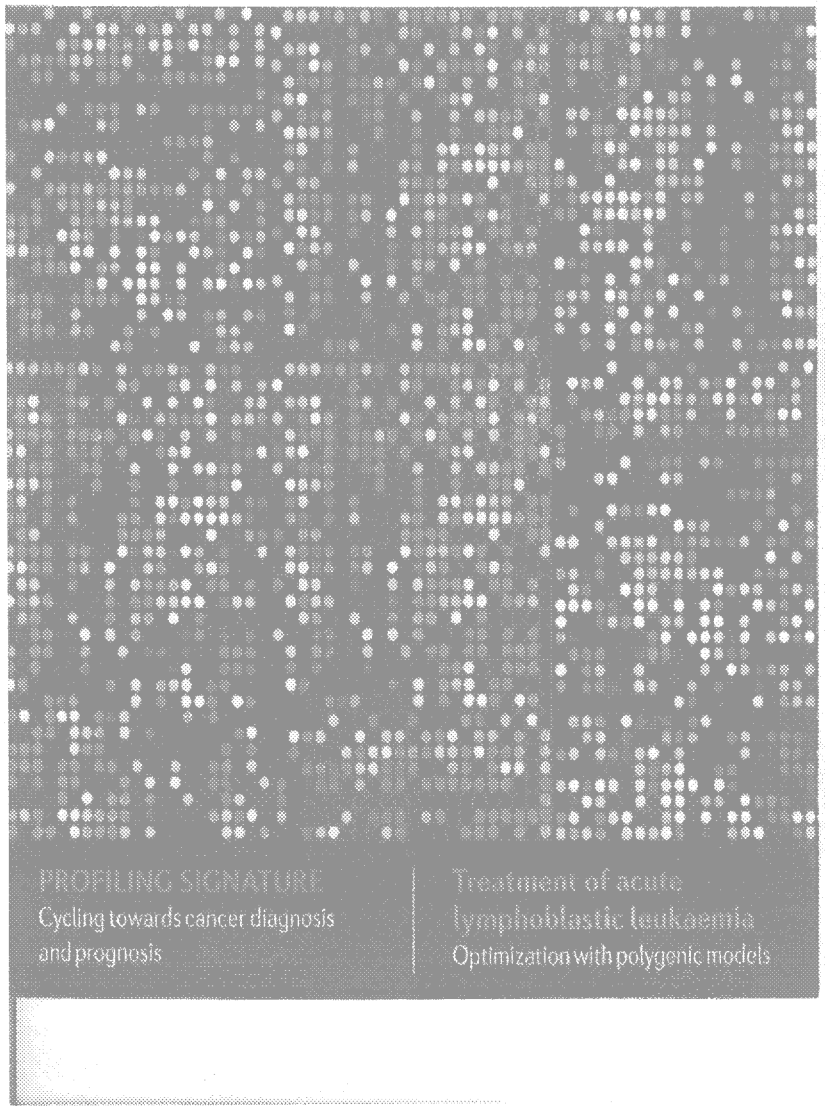
Key Elements of TCC

- All cancer patients consent to a lifetime research project
- Tissues and Genetic Signatures
- Trials and Pipeline Drugs
- Quality Improvement and EBM
- Investment of personnel & technology
- Partnerships with patients, physicians, academia, community, biotech, big pharma: "enterprise" effort

nature
REVIEWS
february 2006 volume 6 no. 2
www.nature.com/reviews

FOCUS Biomarkers

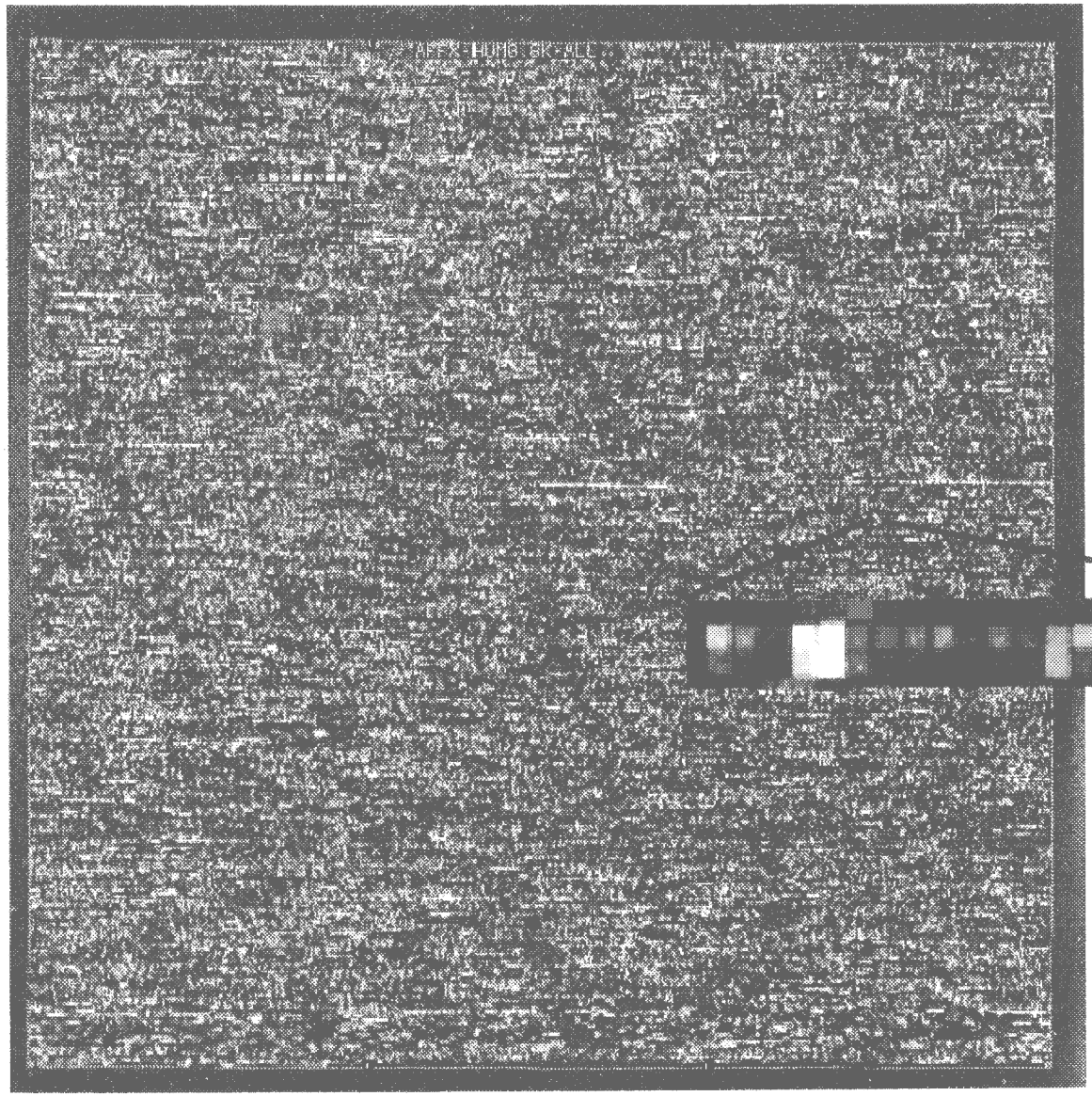
CANCER



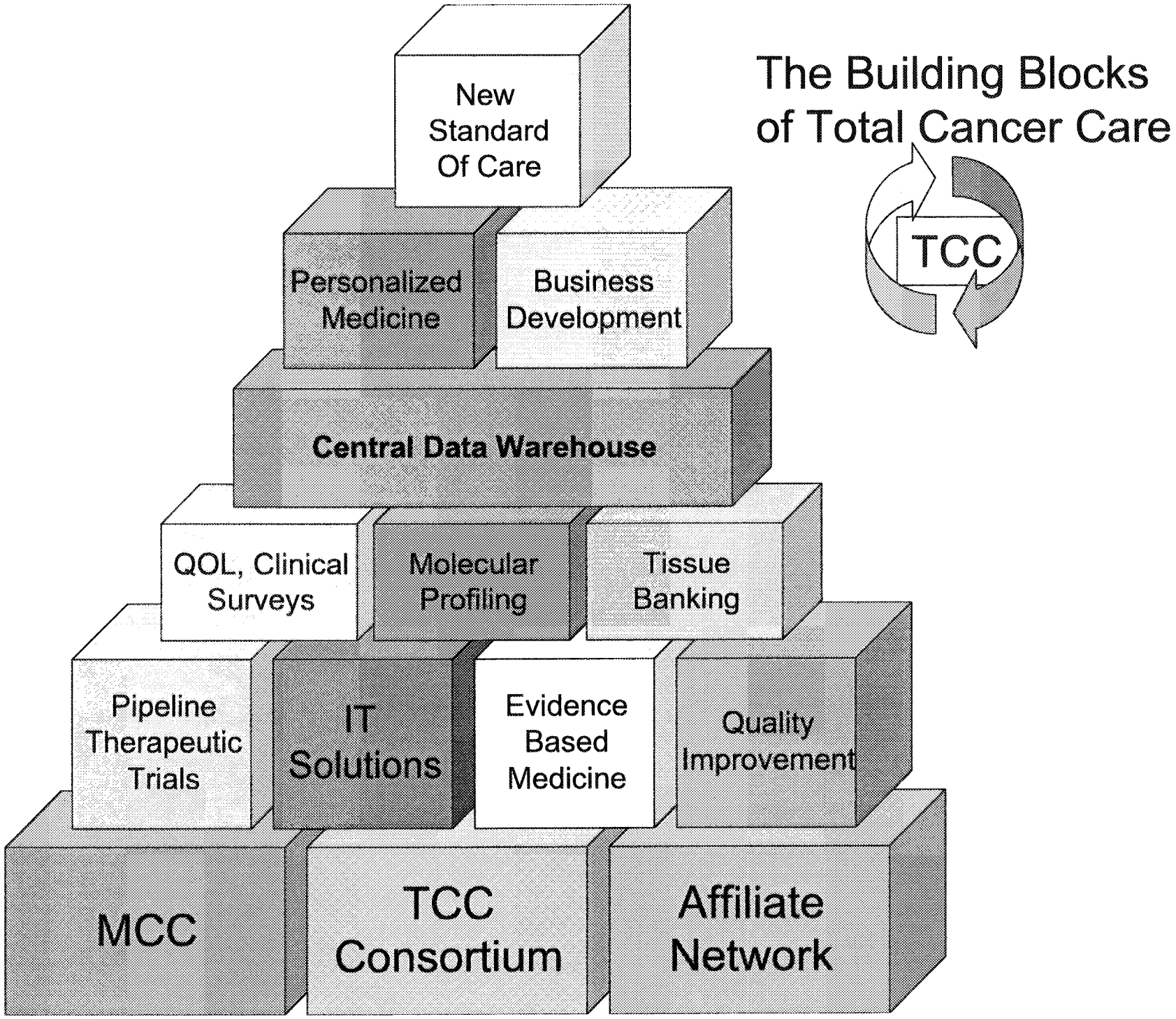
PROFILING SIGNATURE
Cycling towards cancer diagnosis and prognosis

Treatment of acute lymphoblastic leukaemia
Optimization with polygenic models

Affymetrix
Discovery Platform



52K elements
Whole Genome


The Building Blocks of Total Cancer Care
TCC
New Standard Of Care
Personalized Medicine
Business Development
Central Data Warehouse
QOL, Clinical Surveys
Molecular Profiling
Tissue Banking
Pipeline Therapeutic Trials
IT Solutions
Evidence Based Medicine
Quality Improvement
MCC
TCC Consortium
Affiliate Network

Promise of TCC Approach

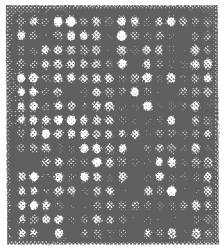
- Old Approach:
  - New Phase II drug
  - Patients randomly selected fro trial
  - Hope for 3 responses out of 30 pts
- New Approach:
  - New Phase II drug—identify target
  - Identify patients harboring target in TCC database
  - Accrue 30 pts harboring target
  - Potential to speed and enhance drug registration

5 Years in the Future

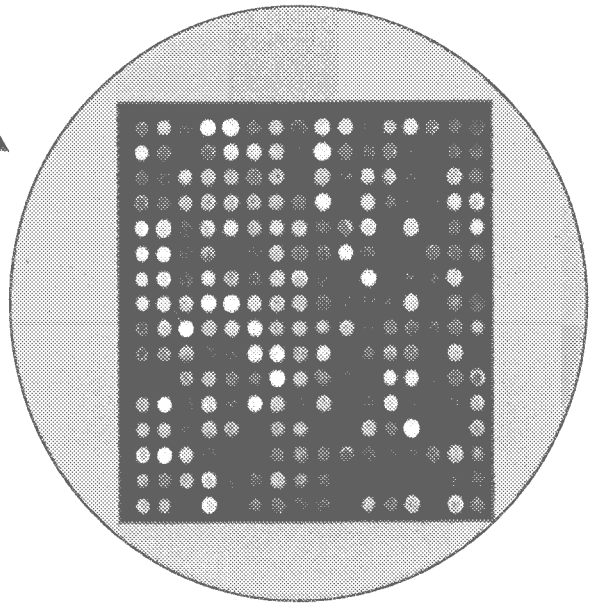
One Tumor, One Chip™

Vision for Future

Tumor Biopsy: Maximize Knowledge



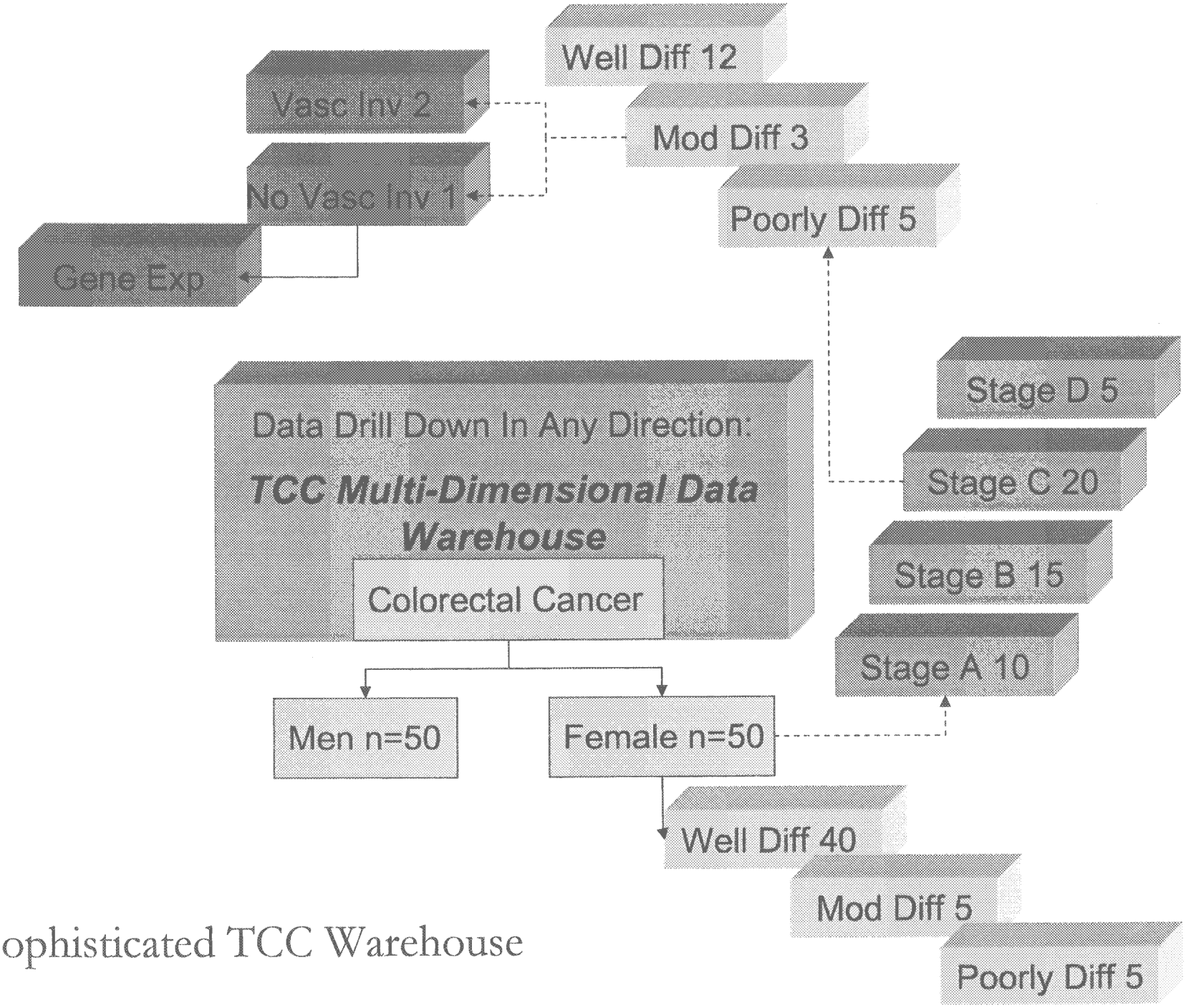
Central Library



Diagnosis:
Colon Cancer

Chemotherapy:
ILF Sensitive 95%

Prognosis:
Poor



Sophisticated TCC Warehouse

Three Portals to Data

Patient View

Researcher View

Clinical Data (summarized)

Clinical Data

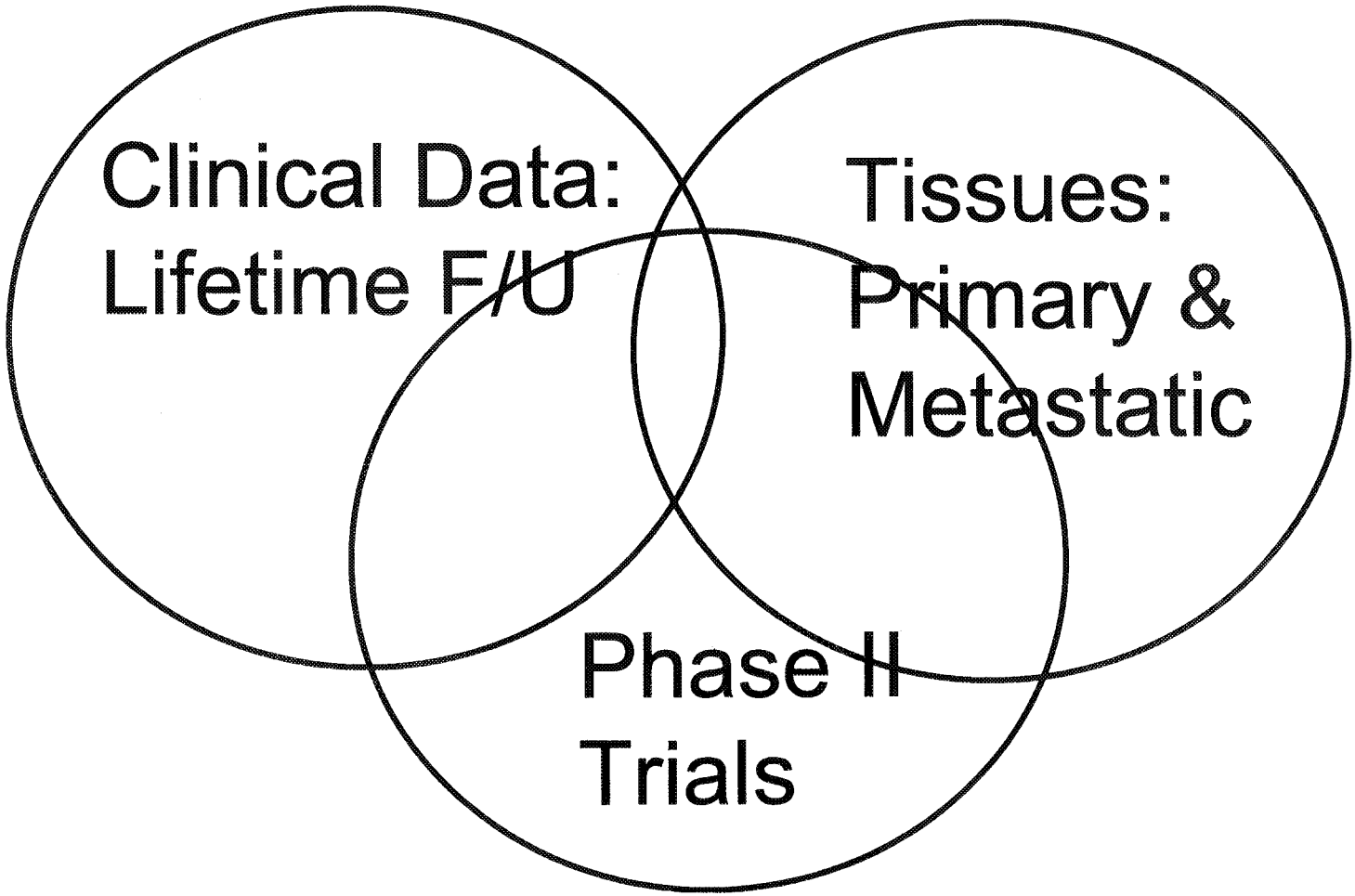
Dicom Archive

Gene Expression

Clinical Data

Touch Screen Technology

No One Has Done It Right

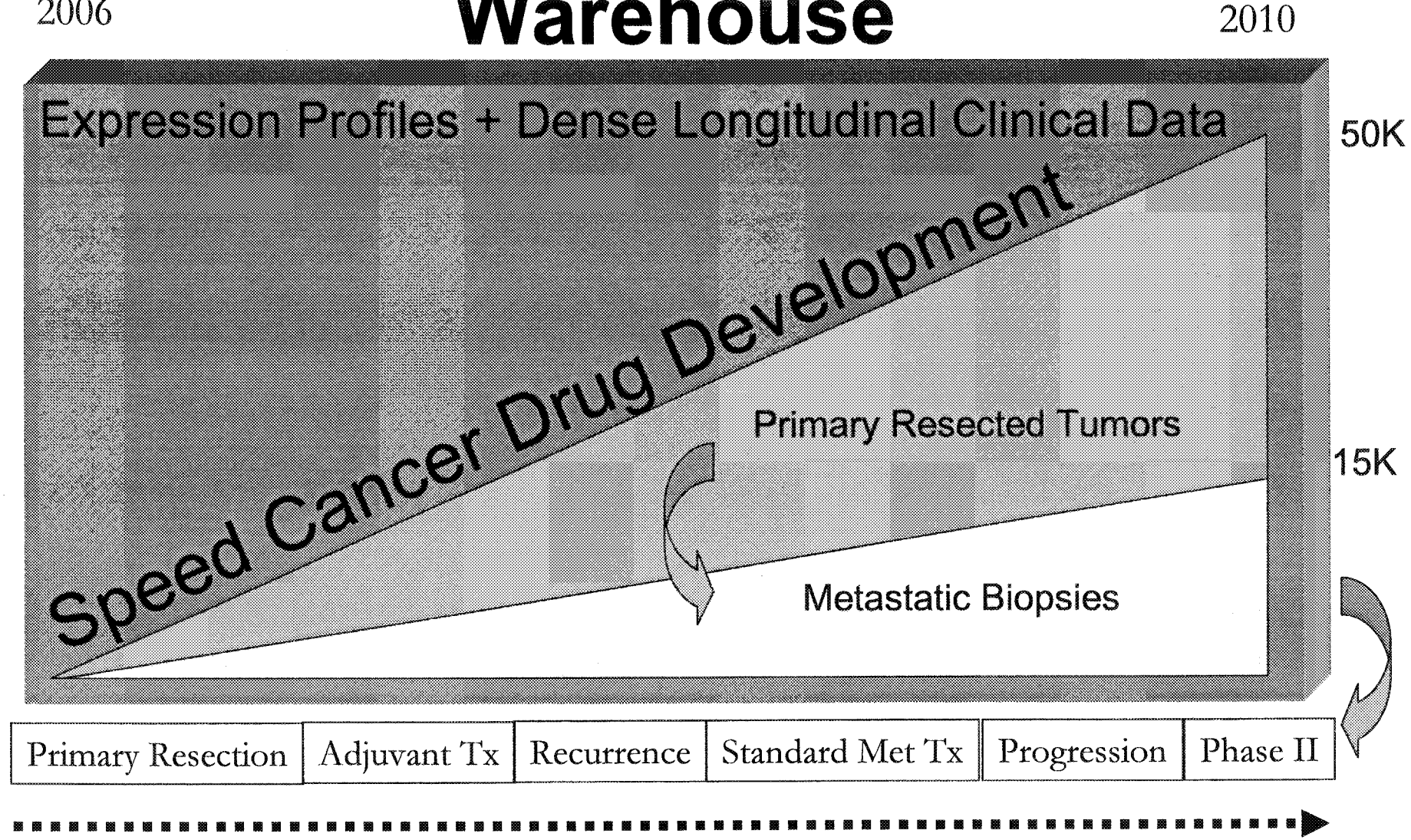


100% Electronic
Web Enabled

Phases

- Phase I (Underway)
  - Demonstrate TCC clinical data and tissue/blood can be collected from MCC and 3 community affiliate hospitals
  - Introduce and test touch screen tablet PC system
- Phase II (Summer 2006)
  - Develop formal TCC consortium
  - Initiate TCC protocol at ~ 8 sites
  - Expand to collect metastatic biopsies (interventional radiology)
  - Initiate multiple Phase II trials
  - Enrich trials with patients harboring appropriate targets

The World's Largest Biorepository and Data Warehouse



TCC Consortium 5-Yr Goals

- Collect, process, and array 50,000 primary tumors & 15,000 metastatic tumors in 5 years
- Co-opt community and academic centers statewide
- Establish multi-dimensional gene expression database with deep clinical annotation: 65,000 tumors x 54,000 genes x 500 clinical endpoints
- Initiate and accrue to 10 or more Phase II pipeline trials enriched with patients harboring targets
- Develop molecular signatures for diagnosis, prognosis, and response to therapy
- Establish THE validation test set for cancer
- Identify new business interests in vast data set

Moon Shot Spin-offs of TCC

- New Investments in State
  - Big Pharma (realized)
  - Biotech (realized)
  - Information Technology linking hospitals and physicians
- Improved Standard of Medical Care
  - Technology advances
  - State of the art clinical trials delivered to community
- Evidence Based Medicine/ Quality Improvement
- Decrease time to new drug registration
- "Resurrection" of shelved therapeutics
- Potential for Reduced Health Care Costs
  - Target therapies to "right patients at the right time"
  - Molecular tests may reduce need for surgical staging
- TCC models extendable to other diseases

Biotech Boom in Tampa

- Brand new incubator space on Moffitt/USF campus
- Burgeoning opportunity for biotech development linked to TCC Data Warehouse
  - Informatics
  - Computer science
  - Genomics
  - Proteomics